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Dr. Michael Shelby, Director – CERHR
NIEHS
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January 15, 2003

Dear Dr. Shelby

I have reviewed the draft of the NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of Propylene Glycol. I offer for your consideration the following comments on the Report.

The toxicological profile of propylene glycol has been well characterized and the CERHR Report reflects this position. This material is of low toxicity following acute or repeated exposure. It is neither a mutagenic nor a carcinogenic substance. Although other areas of toxicity were evaluated, the titled focus of the CERHR Report is potential toxicity of propylene glycol to reproduction and fetal development. Propylene glycol does not impair reproductive performance and there is no evidence of histopathological change to the reproductive organs. The effect of propylene glycol on fetal development was evaluated using 4 species (mice, rats, hamsters and rabbits). While the data may suggest mild fetal toxicity at a dose of 1230 mg/kg in rabbits (increased number fetuses having incomplete ossification), the weight of evidence indicates that propylene glycol does not produce significant fetal toxicity. The data for developmental toxicity also clearly indicate that it is not a teratogenic agent.

Lactic acidosis is recognized as a potential effect from propylene glycol exposure and this metabolic process has been well characterized. The metabolic pathways involved in the conversion of propylene glycol to lactic acid have been adequately studied and information in the scientific literature allows the calculation of the dose of propylene glycol necessary to produce clinically significant levels of lactic acid. The metabolism of propylene glycol to lactic acid follows zero order kinetics, i.e. a finite amount of

propylene glycol is converted metabolically to lactic acid per unit of time. This metabolic pathway is saturated at low levels of propylene glycol and this tends to limit the amount of lactic acid produced. Lactic acidosis from propylene glycol is only relevant if large amounts are administered, e.g. in a medicinal preparation.

Sufficient data exist to evaluate the risk to humans from exposure to propylene glycol. Generation of additional data will not substantially improve the assessment of risk to humans from exposure to this chemical. Propylene glycol should be placed in the category of low priority for further toxicological investigation.

Sincerely yours,

Steven J. Barbee

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